

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

- 11/8/04
1. (Withdrawn) A humanized anti-VEGF antibody which binds human VEGF with a K_d value of no more than about $1 \times 10^{-8}M$.
 2. (Withdrawn) A humanized anti-VEGF antibody which binds human VEGF with a K_d value of no more than about $5 \times 10^{-9}M$.
 3. (Withdrawn) A humanized anti-VEGF antibody which has an ED50 value of no more than about 5nM for inhibiting VEGF-induced proliferation of endothelial cells *in vitro*.
 4. (Withdrawn) A humanized anti-VEGF antibody which inhibits VEGF-induced angiogenesis *in vivo*.
 5. (Withdrawn) The humanized anti-VEGF antibody of claim 4 wherein 5mg/kg of the antibody inhibits at least about 50% of tumor growth in an A673 *in vivo* tumor model.
 6. (Withdrawn) The humanized anti-VEGF antibody of claim 1 having a heavy chain variable domain comprising the following hypervariable region amino acid sequences: CDRH1 (GYX₁FTX₂YGMN, wherein X₁ is T or D and X₂ is N or H; SEQ ID NO:128), CDRH2 (WINTYTGEPTYAADFQR; SEQ ID NO:2) and CDRH3 (YPX₁YYGX₂SHWYFDV, wherein X₁ is Y or H and X₂ is S or T; SEQ ID NO:129).
 7. (Withdrawn) The humanized anti-VEGF antibody of claim 6 comprising the amino acid sequence of SEQ ID NO:7.

8. (Withdrawn) The humanized anti-VEGF antibody of claim 6 having a heavy chain variable domain comprising the following hypervariable region amino acid sequences: CDRH1 (GYTRITNYGMN; SEQ ID NO:1), CDRH2 (WINTYTGEPTYAADFKR; SEQ ID NO:2) and CDRH3 (YPHYYGSSHWYFDV; SEQ ID NO:3).

9. (Withdrawn) The humanized anti-VEGF antibody of claim 1 having a light chain variable domain comprising the following hypervariable region amino acid sequences: CDRL1 (SASQDISNYLN; SEQ ID NO:4), CDRL2 (FTSSLHS; SEQ ID NO:5) and CDRL3 (QQYSTVPWT; SEQ ID NO:6).

11/8/04
10. (Withdrawn) The humanized anti-VEGF antibody of claim 9 comprising the amino acid sequence of SEQ ID NO:8.

11. (Withdrawn) The humanized anti-VEGF antibody of claim 1 having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:7 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:8.

12. (Withdrawn) An anti-VEGF antibody light chain variable domain comprising the amino acid sequence:

DIQX₁TQSPSSLSASVGDRVTTCSASQDISNYLNWYQQKPGKAPKVLITYFTSSLHSGVPS
RFGSGSGTDFLTISLQPEDFATYYCQQYSTVPWTFGQGTKVEIKR (SEQ ID NO:124),
wherein X₁ is M or L.

13. (Withdrawn) An anti-VEGF antibody heavy chain variable domain comprising the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAASGYX₁FTX₂YGMNWVRQAPGKGLEWVGWINTYT
GEPTYAADFKRRFTFSLDTSKSTAYLQMNSLRAEDTAVYYCAKYPX₃YYGX₄SHWYFD

VWGQGTLVTVSS (SEQ ID NO:125), wherein X_1 is T or D; X_2 is N or H; X_3 is Y or H and X_4 is S or T.

- 11/2/04
14. (Withdrawn) A variant of a parent anti-VEGF antibody, wherein said variant binds human VEGF and comprises an amino acid substitution in a hypervariable region of a heavy chain variable domain of said parent antibody.
 15. (Withdrawn) The variant of claim 14 wherein said parent antibody is a human or humanized antibody.
 16. (Withdrawn) The variant of claim 14 which binds human VEGF with a K_d value of no more than about $1 \times 10^{-8}M$.
 17. (Withdrawn) The variant of claim 14 which binds human VEGF with a K_d value of no more than about $5 \times 10^{-9}M$.
 18. (Withdrawn) The variant of claim 14 wherein the substitution is in CDRH1 of the heavy chain variable domain.
 19. (Withdrawn) The variant of claim 14 wherein the substitution is in CDRH3 of the heavy chain variable domain.
 20. (Withdrawn) The variant of claim 14 which has amino acid substitutions in both CDRH1 and CDRH3.
 21. (Withdrawn) The variant of claim 14 which binds human VEGF with a K_d value less than that of said parent antibody.

22. (Withdrawn) The variant of claim 14 which has an ED50 value for inhibiting VEGF-induced proliferation of endothelial cells *in vitro* which is at least about 10 fold lower than that of said parent antibody.
23. (Withdrawn) The variant of claim 18 wherein the CDRH1 comprises the amino acid sequence: GYDFTHYGMN (SEQ ID NO:126)
24. (Withdrawn) The variant of claim 19 wherein the CDRH3 comprises the amino acid sequence: YPYYYGTSHWYFDV (SEQ ID NO:127).
25. (Withdrawn) The variant of claim 14 wherein the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO:116.
26. (Withdrawn) The variant of claim 25 further comprising the light chain variable domain amino acid sequence of SEQ ID NO:124.
27. (Withdrawn) The variant of claim 26 comprising the light chain variable domain amino acid sequence of SEQ ID NO:115.
28. (Withdrawn) The humanized anti-VEGF antibody of claim 1 which is a full length antibody.
29. (Withdrawn) The humanized anti-VEGF antibody of claim 28 which is a human IgG.
30. (Withdrawn) The humanized anti-VEGF antibody of claim 1 which is an antibody fragment.
31. (Withdrawn) The antibody fragment of claim 30 which is a Fab.

11/5/04
32. (Withdrawn) A composition comprising the humanized anti-VEGF antibody of claim 1 and a pharmaceutically acceptable carrier.

33. (Withdrawn) A composition comprising the variant anti-VEGF antibody of claim 14 and a pharmaceutically acceptable carrier.

1 34. (Previously presented) Isolated nucleic acid encoding a humanized variant of a parent anti-VEGF antibody which parent antibody comprises non-human variable domains, wherein said humanized variant binds human VEGF and comprises the following heavy chain Complementary Determining Region (CDR) amino acid sequences: SEQ ID NO:128 as CDRH1, SEQ ID NO:2 as CDRH2 and SEQ ID NO:129 as CDRH3.

2 35. (Previously presented) A vector comprising the nucleic acid of claim 34.

3 36. (Currently Amended) An isolated host cell comprising the vector of claim 35.

4 37. (Previously presented) A process of producing a humanized anti-VEGF antibody comprising culturing the host cell of claim 36 so that the nucleic acid is expressed.

5 38. (Previously presented) The process of claim 37 further comprising recovering the humanized anti-VEGF antibody from the host cell culture.

39. (Withdrawn) A method for inhibiting VEGF-induced angiogenesis in a mammal comprising administering a therapeutically effective amount of the humanized anti-VEGF antibody of claim 1 to the mammal.

40. (Withdrawn) The method of claim 39 wherein the mammal is a human.

41. (Withdrawn) The method of claim 39 wherein the mammal has a tumor.

42. (Withdrawn) The method of claim 39 wherein the mammal has a retinal disorder.

6 43. (Previously presented) The isolated nucleic acid of claim 34, wherein the humanized variant further comprises the following light chain Complementary Determining Region (CDR) amino acid sequences: SEQ ID NO:4 as CDRL1, SEQ ID NO:5 as CDRL2 and SEQ ID NO:6 as CDRL3.

7 44. (Previously presented) The isolated nucleic acid of claim 43, wherein the humanized variant comprises a heavy chain variable domain sequence of SEQ ID NO:7 and a light chain variable domain sequence of SEQ ID NO:8.

8 45. (Previously presented) The isolated nucleic acid of claim 43, wherein the humanized variant comprises a heavy chain variable domain sequence of SEQ ID NO:116 and a light chain variable domain sequence of SEQ ID NO:115.

9 46. (Previously presented) The isolated nucleic acid of claim 34, wherein the humanized variant comprises a heavy chain variable domain sequence of SEQ ID NO:125.

10 47. (Previously presented) The isolated nucleic acid of claim 43, wherein the humanized variant comprises a light chain variable domain sequence of SEQ ID NO:124.

11 48. (Previously presented) The isolated nucleic acid of claim 34, wherein the humanized variant comprises a CDRH1 sequence of SEQ ID NO:1.

12 49. (Previously presented) The isolated nucleic acid of claim 34, wherein the humanized variant comprises a CDRH1 sequence of SEQ ID NO:126.

~~B50~~ (Previously presented) The isolated nucleic acid of claim ~~34~~, wherein the humanized variant comprises a CDRH3 sequence of SEQ ID NO:3.

~~148~~ 51. (Previously presented) The isolated nucleic acid of claim ~~34~~, wherein the humanized variant comprises a CDRH3 sequence of SEQ ID NO:127.